Med. J. Cairo Univ., Vol. 93, No. 3, Accepted 7/5/2025
DOI: 10.22608/MJCU. 1141-1153, September 2025
www.medicaljournalofcairouniversity.net

A Review of Multiple Sclerosis Diagnostic MRI Guidelines

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Abstract

Background: Magnetic Resonance Imaging (MRI) is central to the diagnosis and management of multiple sclerosis (MS). Conventional MRI sequences such as T2-weighted, T1-weighted, fluid-attenuated inversion recovery (FLAIR), and gadolinium-enhanced scans are well-established in detecting MS lesions and demonstrating dissemination in space and time per diagnostic criteria. However, these standard techniques have limitations, prompting the development of advanced MRI modalities to Improve sensitivity and specificity for MS pathology.

Aim of Study: This review provides a detailed analysis of MRI diagnostic guidelines for MS, comparing traditional sequences with emerging and advanced techniques. We evaluate each modality's strengths, limitations, diagnostic value (sensitivity/specificity), and recommended use cases. Special considerations for pediatric MS imaging are discussed. We aim to furnish neuroimaging researchers, clinicians, and radiologists with an up-to-date reference to inform both clinical practice and future research.

Material and Methods: We systematically reviewed recent consensus guidelines and key studies, published between February 2010 and February 2025, on MS MRI, including the 2017 McDonald criteria and 2021 MAGNIMS–CMSC–NAIMS international recommendations, as well as research on advanced imaging sequences (double inversion recovery, susceptibility-weighted imaging, diffusion tensor imaging, magnetization transfer imaging, 7-Tesla MRI, functional MRI, quantitative susceptibility mapping, myelin water imaging, connectomics, and machine learning-based analyses). Data on lesion detection rates, diagnostic performance, and clinical correlations were extracted to compare modalities.

Results: Conventional MRI at 1.5–3T with T2/FLAIR and gadolinium-enhanced T1 sequences remains the cornerstone for MS diagnosis, offering high sensitivity for white matter lesions but limited specificity for MS pathology. Newer 3D-FLAIR sequences at 3T improve lesion detection, especially in periventricular and cortical regions. Advanced techniques provide incremental benefits: for example, double inversion recovery (DIR) improves cortical lesion visibility by 1.5–5× over FLAIR, and susceptibility-based MRI reveals the central vein sign with high specificity for MS lesions. Ultra-high-field 7T MRI further increases sensitivity for small lesions and cortical pathology. Diffusion and magnetization transfer imaging offer quantitative biomarkers of microstructural damage. At the same time, functional MRI and connectomic analyses shed light on network reorganization in MS.

Conclusion: Conventional sequences, notably 3D-FLAIR and post-contrast T1-weighted imaging, continue to anchor MS diagnostic protocols, while advanced sequences such as DIR and SWI offer valuable adjuncts in complex or research-driven cases. Gadolinium use should be judicious and limited to initial diagnosis and selected monitoring needs. Advanced modalities improve detection of cortical and subtle lesions and provide prognostic insights but require further validation before widespread clinical adoption. Future directions include integrating higher-field imaging, quantitative markers, and AI-based tools into routine practice to enhance diagnostic precision and disease monitoring. This review highlights evidence-based imaging strategies for MS and identifies future directions to enhance MRI's diagnostic and prognostic utility in this disease.

Key Words: *Multiple Sclerosis (MS) – Magnetic Resonance Imaging (MRI) – Diagnostic Guidelines – Conventional MRI Sequences (T1-weighted, T2-weighted, FLAIR, Gadolinium-enhanced) – Advanced MRI Techniques (DIR, SWI, DTI, MTI, 7T MRI, fMRI) – Lesion Detection Diagnostic Performance – McDonald Criteria – MAGNIMS-CMSC-NAIMS Guidelines.*

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Introduction

MULTIPLE sclerosis (MS) is often cited as the second leading cause of neurological impairment in young adults, affecting more than two million people worldwide, a fact that continues to surprise many outside the neurology field. At its core, MS is an acquired, chronic, autoimmune demyelinating disease that directly targets the central nervous system (CNS) [1]. Early stages are typically marked by obvious immune cell attacks, but interestingly, as the disease progresses, the dynamic shifts. Instead of ongoing invasion, the damage is increasingly driven by persistent, low-grade inflammation inside the CNS itself, primarily orchestrated by local glial cells such as astrocytes and microglia [2]. This subtle but critical change in pathology challenges many earlier models of MS and highlights why more sophisticated imaging techniques are urgently needed the disease is simply more complex than it first appears.

Since its introduction in the 1980s, MRI has dramatically reshaped how clinicians diagnose and manage MS [3]. Its impact cannot be overstated: MRI enables the detection of early, often subtle signs of disease activity that would otherwise remain invisible during routine clinical examinations. Such markers cognitive impairment, brain atrophy, and fatigue are crucial for forming a holistic understanding of MS [4]. Not only does MRI facilitate early diagnosis, but it also plays an increasingly central role in monitoring disease progression, evaluating long-term disability accumulation, and identifying transitions to secondary progressive MS all of which guide critical treatment decisions [5]. From a clinical perspective, the ability to track these changes noninvasively is nothing short of transformative.

Conventional MRI sequences including proton density/T2-weighted, T1-weighted, FLAIR, and gadolinium-enhanced T1 imaging have become the mainstay of MS diagnosis and management, primarily due to their sensitivity to white matter lesions and ease of standardization across clinical settings [6]. These sequences are deeply embedded in both diagnostic frameworks and follow-up protocols. Nevertheless, despite their proven utility, they do not capture the full spectrum of MS pathology. Over time, more advanced MRI techniques have been developed to fill these gaps, offering higher specificity for diagnosing MS and, potentially, providing new prognostic biomarkers. Emerging modalities capable of visualizing cortical lesions (CL), the central vein sign (CVS), and paramagnetic rim lesions (PRL) represent some of the most promising advancements to date [7]. From a research standpoint, integrating these newer imaging markers into clinical practice could open new avenues for earlier and more precise interventions.

This review is structured to first explore the diagnostic contributions of traditional MRI sequences in MS, with a focus on their current applications as outlined in prevailing clinical guidelines. Following that, we will compare conventional techniques with newer, more specialized imaging approaches, critically examining the strengths and limitations of each. By presenting a side-by-side analysis of sensitivity, specificity, and practical application, we aim to provide a more precise roadmap for clinicians navigating the increasingly complex landscape of MS imaging.

MRI protocol for multiple sclerosis (MS) diagnosis:

Diagnosing MS has never been straightforward, and the McDonald criteria attempt to bring clarity through two major concepts: Dissemination in Space (DIS) and Dissemination in Time (DIT). DIS refers to MS lesions appearing in separate locations across the CNS, whereas DIT emphasizes the occurrence of lesions at different points in time. According to the 2017 revision, proving DIS can involve either an additional clinical attack or suggestive MRI findings, especially in patients who present with only a single lesion [8]. As for DIT, it can now be demonstrated not only by clinical events or new MRI findings but also by CSF-specific oligoclonal bands even if the patient has had only one attack. I find these criteria a double-edged sword: while they allow earlier diagnosis, they also introduce more gray areas where misdiagnosis might creep in, especially in atypical cases.

Significantly, the McDonald criteria have evolved into a broader diagnostic tool that goes beyond clinical observations, incorporating radiographic and laboratory evidence, especially MRI findings [9]. This integration has unquestionably improved the sensitivity and timeliness of MS diagnosis, enabling earlier therapeutic interventions, which can be crucial in slowing disease progression. Nevertheless, it is worth remembering that the criteria have undergone several revisions since they were first introduced in 2001, culminating most recently in the 2017 update [10]. Each iteration has aimed to sharpen diagnostic precision, but whether we have reached the optimal balance between sensitivity and specificity remains an open question.

The evolution of these criteria has not occurred In a vacuum. The 2015 MAGNIMS and 2016 CMSC guidelines had a considerable impact, par-

ticularly in standardizing MRI protocols and striving for greater diagnostic accuracy in MS [12]. Their recommendations directly influenced the 2017 McDonald revisions, resulting in a more streamlined clinical application of MRI and a significant improvement in managing patients with clinically isolated syndrome (CIS) [9]. Nevertheless, a word of caution is necessary here: Even with enhanced guidelines, expert clinicians must remain vigilant. Misdiagnosis remains a real risk if alternative conditions are not carefully ruled out a point that, in my view, cannot be emphasized enough [9].

More recently, efforts to unify global standards for MS imaging have culminated in the 2021 MAGNIMS–CMSC–NAIMS consensus recommendations. This collaboration among major international organizations has produced a comprehensive set of standardized MRI protocols designed to improve not only diagnosis but also prognosis and long-term monitoring [11]. Translating cutting-edge MRI research into actionable clinical practice has been a significant step forward. However, I suspect that widespread adoption may take longer than anticipated, given the variability in MRI access and expertise worldwide.

Interestingly, at the 40th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) held in 2024, a new update to the McDonald criteria was presented. While full details await peer-reviewed publication, early indications suggest that further refinements aim to strike an even finer balance between early diagnosis and diagnostic accuracy [12]. It will be fascinating to see whether these upcoming changes will address lingering concerns or introduce new debates within the MS community.

Conventional MRI in MS: Sequences, Diagnostic Criteria, and Limitations:

Conventional MRI, which is shown in Table 1, remains the workhorse diagnostic criterion and routine follow-up imaging of MS. The MAGNIMS and CMSC guidelines from 2015-2016 recommended using axial T2-weighted, dual-echo T2-weighted, axial and sagittal T2-FLAIR, and contrast-enhanced T1-weighted sequences, preferably at 3T [13]. The 2017 revisions of the McDonald diagnostic criteria for multiple sclerosis (MS) maintain consistency with previously recommended MRI protocols [14]. While 3T MRI detects more T2 brain lesions compared to 1.5T, this increased sensitivity does not significantly affect the fulfillment of DIS or DIT criteria or subsequent MS diagnosis [15].

However, conventional MRI has limitations in its specificity for MS pathology. The correlation between conventional MRI lesion measures and clinical status is weak, and there is a risk of misdiagnosis due to overlapping radiological patterns with other CNS inflammatory disorders [16]. Additionally, conventional MRI is less sensitive in detecting cortical lesions and spinal cord involvement, which are important aspects of MS pathology [3].

T2-Weighted and FLAIR Imaging Sequences – Lesion Identification:

T2-weighted and FLAIR imaging remain fundamental for detecting MS lesions, particularly in the white matter. However, these conventional sequences have limitations in detecting cortical and subpial lesions [17].

T2-weighted sequences:

The 2017 McDonald criteria defined lesions in multiple sclerosis (MS) as areas of hyperintensity on T2-weighted or proton-density-weighted MRI scans that are at least 3mm in long axis. This definition helps standardize the T2-weighted sequences as fundamental in MS diagnosis. T2-weighted imaging is highly sensitive for detecting MS lesions, which appear as hyperintense areas on T2-weighted scans [18]. They can detect diffusely abnormal white matter (DAWM), which is present in at least 25% of MS patients and is associated with higher lesion volume, reduced brain volume, and earlier conversion to MS in clinically isolated syndrome cases [19].

T2-weighted imaging may have limitations in certain aspects of MS lesion characterization. For instance, a study using texture analysis found that T2-weighted images did not show significant predictive ability in differentiating acute from chronic MS lesions, unlike susceptibility-weighted imaging (SWI) [20]. However, this does not diminish the overall importance of T2-weighted sequences in MS imaging.

The Fluid-Attenuated Inversion Recovery (FLAIR) imaging technique:

FLAIR further improves lesion visibility by suppressing the cerebrospinal fluid (CSF) signal, which enhances contrast between lesions and surrounding tissues, making lesions more conspicuous. This is particularly useful for detecting periventricular and cortical/juxtacortical lesions in MS [21]. Sagittal FLAIR is particularly adept at depicting Dawson's finger lesions along the corpus callosum (a hallmark pattern in MS). It is consid-

ered the core sequence for MS diagnosis and monitoring due to its high sensitivity [22].

Indeed, High-resolution 3D FLAIR improves the detection of brain lesions in MS patients compared to conventional 2D sequences [23]. The isotopic ~1mm resolution allows for better visualization of small lesions and provides more detailed anatomical information. When high-quality 3D FLAIR scans (preferably at 3 T) are available, additional T2- T2-weighted sequences are no longer mandatory, as indicated with the 2021 MAGNIMS–CMSC– NAIMS [14].

However, traditional 3D FLAIR sequences often require long acquisition times, which can be a limitation in clinical settings. Compressed sensing techniques have been applied to 3D FLAIR imaging to address this issue. A study showed that compressed sensing 3D FLAIR preserved diagnostic performance for MS plaque detection while reducing scan time by 27% [24]. The image quality and number of detected MS lesions were similar between conventional and compressed sensing FLAIR acquisitions.

Interestingly, recent research has explored the potential of using 3D FLAIR for brain volumetry in MS patients. A study found that brain volumes derived from 3D FLAIR images showed similar relationships to disability and cognitive dysfunction as those derived from 3D T1 images [25]. This suggests that 3D FLAIR could potentially serve dual purposes in MS imaging protocols – lesion detection and brain volumetry.

T1-weighted imaging and gadolinium enhancement – activity and "black holes":

T1-weighted MRI provides complementary information to T2/FLAIR [26]. Pregadolinium T1 images show the baseline anatomy and existing lesions, while post-gadolinium T1 images reveal active inflammatory lesions that enhance due to blood-brain barrier disruption. Gadolinium-enhancing lesions on T1-weighted images are critical for detecting active disease in MS patients and are highly recommended by the 2021 MAGNIMS–CMSC–NAIMS consensus recommendations if a new suspicious lesion is detected on surveillance MRI2 and in the follow-up of PML lesions for early detection and monitoring of inflammatory PML and PML-immune reconstitution inflammatory syndrome. These lesions reflect acute inflammation and blood-brain barrier disruption, providing valuable information for diagnosis and disease monitoring [27].

The use of pre- and post-contrast T1-weighted images, along with FLAIR, has shown high accuracy (87.7%) in detecting and categorizing MS lesions [28]. However, recent studies have raised concerns about gadolinium retention in brain tissues after multiple administrations of gadolinium-based contrast agents (GBCAs) [29]. This has led to recommendations from regulatory agencies to restrict GBCA use to clinically necessary situations [18]. Interestingly, some studies have questioned the necessity of gadolinium administration in routine follow-up imaging of MS patients. A study of 507 follow-up MRI scans found that the use of contrast-enhanced T1 images did not change the diagnosis of interval disease progression compared to non-enhanced sequences when using advanced techniques like subtraction maps [30]. This suggests that in some cases, non-contrast MRI may be sufficient for monitoring MS progression.

Short tau inversion recovery technique (STIR):

STIR sequences are widely applied in magnetic resonance imaging (MRI) for the detection of lesions for multiple sclerosis (MS), as clearly detailed within the spinal cord protocol [14]. The available body of research confirms the greater efficiency of STIR sequences over conventional imaging methods for spinal cord lesion detection [31]. Additionally, these sequences can show clinical utility within some scenarios, for example, the use of 2D or 3D imaging within the optic nerve MRI protocol [14].

Although STIR is beneficial for the assessment of spinal cord lesions, it is not as effective for brain imaging for multiple sclerosis. Other sequences, including fluid-attenuated inversion recovery (FLAIR), double inversion recovery (DIR), and phase-sensitive inversion recovery (PSIR), are more effective for locating cortical and white matter lesions of the brain [32]. This highlights the importance of using a range of MRI sequences to allow for accurate determination and ongoing monitoring of multiple sclerosis.

The Short Tau Inversion Recovery (STIR) sequence, implemented on a three-dimensional (3D) platform, has been shown to be highly effective at detecting spinal cord lesions in subjects with multiple sclerosis. Comparative assessment of a reference data set consisting of 3D STIR versus a Phase-Sensitive Inversion Recovery (PSIR) protocol applied on a 3D platform showed PSIR to detect substantially more lesions (371 versus 173) [33]. This implies that while 3D STIR is useful, more advanced imaging modalities like 3D PSIR might have superior detection capabilities for lesions. Recent studies focused on developing virtual

STIR (vSTIR) images using T1- and T2-weighted imaging modalities without contrast agents through artificial intelligence algorithms. Direct comparison between vSTIR and accurate STIR images confirmed that vSTIR was concordant with accurate STIR results for 13 of 15 evaluated categories, potentially allowing for shorter examination times and improved throughputs **[34]**. The spinal cord MRI protocol requires the employment of proton density-weighted imaging or STIR sequences for confirmation of lesions and artefact reduction, since a single T2-weighted imaging alone is not adequate, aligning with the consensus recommendations put forth by MAGNIMS–CMSC–NAIMS for the year 2021 **[14]**. Coronado et al. **[32]** describe the use of proton density-weighted images together with FLAIR, T2-weighted, and pre-/post-contrast T1-weighted images within their deep learning framework for segmenting lesions **[35]**. This highlights that proton density imaging adds supplementary.

Proton density-weighted:

In the spinal cord MRI protocol, PD-weighted imaging, alternatively with STIR, is required to confirm the presence of lesions and exclude artifacts, as the single acquisition of a T2-weighted image is not sufficient alone, according to the 2021 MAGNIMS–CMSC–NAIMS consensus recommendations **[14]**. Coronado et al. **[32]** mention using PD-weighted images along with FLAIR, T2-weighted, and pre-/post-contrast T1-weighted images in their deep learning model for enhancing lesion segmentation **[35]**. This suggests PD imaging provides complementary information for lesion detection.

Table (1): Conventional MRI Sequences in MS – Diagnostic Value and Use.

MRI Sequence	Diagnostic Value	Typical Use in MS
T1-weighted (pre-contrast)	- Identifies hypointense lesions (‘black holes’) indicating axonal loss or chronic lesions.	- Assessment of chronic tissue damage.
T1-weighted (post-contrast)	- Highlights areas with active blood-brain barrier disruption.	- Detection of active inflammation or new lesions.
T2-weighted	- Shows total lesion load including old and new lesions.	- General detection and quantification of MS lesions.
FLAIR (Fluid-Attenuated Inversion Recovery)	- Suppresses CSF signal to better visualize periventricular and cortical lesions.	- Detection of lesions near ventricles and in cortex; sensitive for MS plaques.
Proton Density (PD)	- Differentiates between gray and white matter; detects subtle lesions.	- Helpful in early lesion detection, especially in brainstem or spinal cord.
STIR (Short Tau Inversion Recovery)	- Suppresses fat signal; useful in spinal cord imaging.	- Detection of spinal cord lesions in MS.

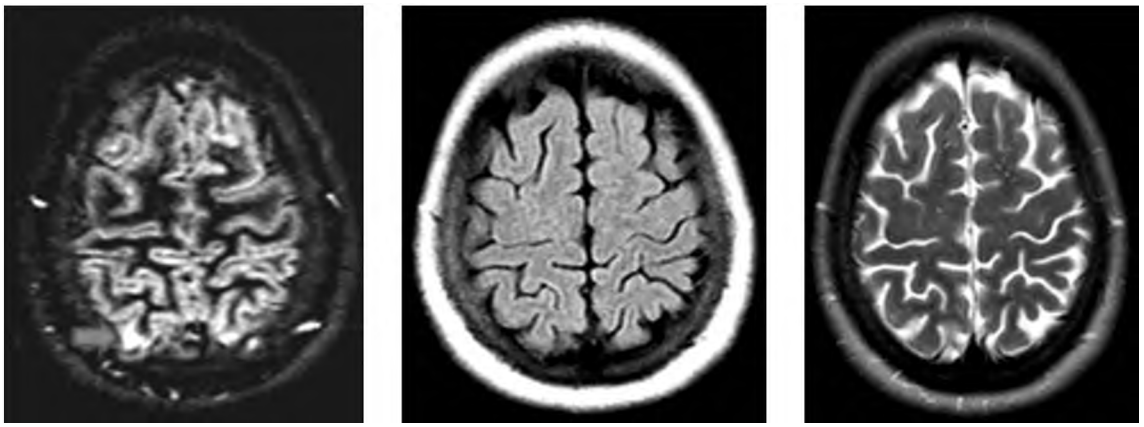
Advanced and Emerging MRI Techniques in MS:

To address the well-documented discrepancy between clinical and conventional MRI (fMRI), advanced MRI techniques overcome the limitations of conventional methods by offering new MR markers that are more closely associated with the most disabling pathological features of multiple sclerosis (MS).

Double Inversion Recovery (DIR) – Highlighting Cortical Lesions:

Double inversion recovery is a pulse sequence that applies two inversion pulses to suppress signals from both white matter and cerebrospinal fluid, effectively “nulling out” those tissues and leaving lesions (particularly in gray matter) more conspicuous. In MS, DIR has been shown to significantly improve detection of Cortical and juxtacortical lesions compared to conventional T2 or FLAIR **[36]**. Specifically, DIR was found to have a sensitivity of 22.8% for detecting histopathologically-validated cortical lesions, compared to only 5.4% for both T2 and FLAIR sequences **[38]**. This represents a significant improvement, although it still detects less than a quarter of all cortical lesions. DIR also showed higher specificity (91.1%) compared to T2 and FLAIR (75-80%) **[37]**. Another Studies indicate that DIR can be 1.5 to 5 times more sensitive than traditional MRI for cortical lesion identification **[36]**. For example, an MS patient might have several intracortical lesions visible on DIR that were not seen on FLAIR or T2 (FLAIR is limited in pure cortex since lesion and surrounding cortex both appear hyperintense). Fig. (1) illustrates such a case: A small intracortical lesion (arrow) is evi-

dent on DIR (Panel A), whereas it is inapparent on the corresponding FLAIR (B) and T2 (C) images. By improving the visualization of gray matter involvement, DIR contributes to a more complete assessment of disease burden. Indeed, cortical lesions are now recognized as a frequent occurrence even in early MS and are linked to cognitive dysfunction and disability progression.



(A) (B) (C)

Fig. (1): Comparison of MRI sequences for cortical lesion detection. (A) An axial DIR image of an MS patient shows a small intracortical lesion in the right parietal cortex (green arrow). (B) The same slice on axial FLAIR and (C) axial T2-weighted imaging – the cortical lesion is not apparent on these conventional sequences. DIR's suppression of normal white matter and CSF makes the cortical plaque visible.

While DIR improves cortical lesion detection, it still has limitations. Even with DIR, only about 18% of histopathologically-confirmed cortical lesions are detected at clinical field strengths *[37]*. The improved contrast of DIR comes at the expense of lower signal-to-noise ratio (SNR) and resolution challenges. DIR images often appear noisier and can suffer from more artifacts (e.g., from motion or B1 inhomogeneity). The increased susceptibility to artifacts in DIR images is partly due to the complex acquisition process involving multiple inversion pulses. Motion artifacts, in particular, can be problematic for DIR sequences. Eichinger et al. (2019) note that conventional DIR showed significantly more definite artifacts within the white matter (p=0.024) and highly significantly more at the cortical-sulcal interface (p<0.001) compared to a compressed sensing (CS) accelerated DIR sequence *[31]*. However, DIR remains one of the most sensitive sequences available for cortical lesion visualization in MS at 3 T. Newer techniques like compressed sensing DIR show promise for maintaining diagnostic quality while reducing scan time *[31]*.

Susceptibility-Weighted Imaging (SWI):

Central Veins and Iron Rims Susceptibility-weighted imaging (SWI) has significantly enhanced the detection and characterization of multiple sclerosis (MS) lesions compared to conventional MRI sequences. SWI evolved from simple 2D T2*-weighted sequences to 3D sequences with improved spatial resolution and enhanced susceptibility contrast, making it highly sensitive to compounds that distort the local magnetic field, such as iron and calcium *[38]*.

In MS, SWI has proven particularly useful for identifying the central vein sign and peripheral rim sign in lesions, which are not visible on standard T2*-weighted images *[38]*. These features can help differentiate MS from other neurological conditions. For instance, paramagnetic rims around brain lesions were found in 81.2% of MS patients compared to only 4.8% of neuromyelitis optica spectrum disorder patients in one study using 3T MRI *[39]*. SWI has also shown promise in detecting cortical lesions, especially subpial lesions, which are poorly visualized on conventional MRI sequences. A novel sequence called IR-SWIET (inversion recovery susceptibility weighted imaging with enhanced T2 weighting) demonstrated superior sensitivity in detecting subpial lesions compared to other 3T methods *[17]*. Additionally, SWI at ultra-high field strength (7T) has revealed new imaging signs related to improved magnitude and phase contrast imaging, potentially facilitating the detection of inconspicuous epileptogenic lesions in drug-resistant epilepsy patients *[40]*. SWI and related techniques show promise in improving MS di-

agnosis and monitoring. Studies have demonstrated high sensitivity and specificity for MS diagnosis using CVS assessment, particularly at higher field strengths like 7T MRI **[41]**. However, further validation and standardization are needed before these techniques can be fully integrated into routine clinical practice for MS management **[42].**

Not all MRI centers routinely acquire SWI for MS patients, though many now include at least a T2*-weighted sequence for brain imaging **[38].** The imaging appearance of SWI strongly depends on the acquisition technique, which can vary across MRI vendors and sequences **[38]**. Poor image quality can lead to missed identification of tiny central veins, which are key features in MS lesions **[43].** Interpretation of SWI requires expertise and standardization. Correct application of the central vein sign (CVS) necessitates appropriate imaging parameters, such as 3mm slices or high-resolution 3D images, as thicker slices can create false impressions of central veins **[44]**. There is also a need for standardized thresholds to determine what percentage or number of lesions with CVS constitutes a "positive" test for MS diagnosis **[45].**

Diffusion Tensor Imaging (DTI) and Diffusion-Based Techniques – Microstructural Insights:

Diffusion MRI tracks the movement of water molecules in tissue, which is shaped by the microstructure. The most often used technique is Diffusion Tensor Imaging (DTI), which models water diffusion in terms of amplitude and directionality (anisotropy). Intact axonal fibres in the CNS white matter limit water transport across them, hence causing significant anisotropy. Demyelination or axonal loss causes diffusion to be less directed. Among the main DTI measurements are mean diffusivity (MD), which rises in damaged white matter, and fractional anisotropy (FA), which is lower in damaged white matter.

Magnetization Transfer Imaging (MTI) – Myelin Quantification:

Magnetization Transfer Imaging (MTI) represents one of the more exciting developments in MS research, at least in my view. Since Dousset et al.'s pioneering work, MTI has offered a way to generate contrast in MR images that reveals far more than conventional imaging could **[46]**. The ability of MTI techniques like magnetization transfer ratio (MTR) and quantitative magnetization transfer (qMT) parameters to reflect myelin content and subtle microstructural changes gives clinicians a critical tool not only for diagnosis but also gives some insight about the degree of tissue damage **[47]**. The fact that MTI can detect tissue changes up to four months before lesions become visible on regular MRI is, frankly, a game-changer although it is worth asking why wider clinical adoption has been so slow.

Still, MTI has its limitations, and ignoring them would be a mistake. For example, even though MTR showed promising sensitivity (78%) for detecting cortical demyelination, its specificity was alarmingly low at 29%, suggesting that factors beyond demyelination might be influencing the readings **[48]**. In practice, this means MTI findings need careful interpretation and, ideally, should be combined with other imaging techniques like diffusion tensor imaging (DTI) to build a more complete picture **[49].** I believe that moving forward, multimodal imaging approaches are the only realistic path if we want to capture the full complexity of MS pathology.

Ultra-High-Field MRI (7 Tesla) – Pushing the Frontiers of Detection:

Ultra-high-field 7 Tesla (7T) MRI has quickly emerged as a transformative tool for both neuroimaging research and clinical applications, particularly in the context of multiple sclerosis (MS). Thanks to its markedly increased signal-to-noise ratio (SNR) and superior spatial resolution, 7T MRI enables far more precise visualization of small anatomical structures and subtle pathological changes than conventional imaging allows **[50]**. In fact, studies have reported up to a 300% improvement in temporal SNR and resting-state functional connectivity coefficients compared to standard 3T MRI, significantly boosting our ability to detect and map functional neural architecture **[51].** For researchers working in MS imaging, the leap in detail offered by ultra-high-field 7T MRI feels both thrilling and, admittedly, a little daunting. The ability to see structures and pathological changes at such satisfactory resolution thanks to markedly improved signal-to-noise ratio (SNR) opens doors that standard imaging simply could not **[50]**. Some studies have reported nearly a 300% gain in temporal SNR and functional connectivity mapping compared to 3T MRI, which, if anything, highlights how much we were probably missing before **[51].** Nevertheless, despite the excitement, practical barriers remain.

Right now, 7T MRI is not standard for MS diagnosis, but the emerging evidence indeed suggests it could become a game-changer. Its higher sensitivity for detecting small or atypical lesions along with better characterization of lesion pathology offers the real possibility of increasing diagnostic specificity and helping to avoid misclassification with

other neurological diseases [52]. What is even more exciting is the growing role of 7T in metabolic imaging. Thanks to its superior spectral resolution, researchers can now resolve metabolites in ways that simply were not feasible before [53]. I find this shift toward metabolic exploration one of the most compelling directions in MS research right now, as it gets us closer to understanding not just where damage occurs, but why.

Beyond structural and metabolic imaging, 7T MRI has also dramatically improved visualization of iron accumulation and leptomeningeal inflammation two markers increasingly recognized as key indicators of disease progression [54]. Having more precise imaging of these processes feels less like an incremental improvement and more like a fundamental shift in how we can monitor the disease. If properly leveraged, these insights might completely reshape our long-term strategies for both diagnosis and management.

That said, no technology comes without a cost and with 7T MRI, the challenges are far from trivial. Technical hurdles like RF field non-uniformity and higher RF energy deposition complicate its use in routine settings [55]. On top of that, the expense remains a considerable obstacle; few institutions can afford a 7T system, leading to creative but imperfect solutions like generating "synthetic 7T" images from 3T scans using AI algorithms. It is an innovative workaround, but at least for now, it does not fully replicate the actual benefits of ultra-high-field imaging. Moving forward, striking a balance between ambition and accessibility will be crucial if we want 7T MRI to become a standard part of MS care rather than a research luxury.

Table (2): Advanced MRI Modalities in MS – Comparative Summary.

MRI Modality	Principle/Technique	Diagnostic Value	Typical Use in MS
- Magnetization Transfer Imaging (MTI)	- Measures exchange of magnetization between free water and macromolecule-bound protons.	- Detects subtle myelin loss even in normal-appearing white matter.	- Assessment of demyelination and remyelination.
- Diffusion Tensor Imaging (DTI)	- Measures directional diffusion of water molecules.	- Identifies microstructural changes and axonal integrity.	- Evaluation of white matter tract damage and connectivity.
- Functional MRI (fMRI)	- Detects brain activity via changes in blood oxygenation (BOLD signal).	- Assesses functional reorganization and compensation.	- Studies cognitive changes and neuroplasticity.
- MR Spectroscopy (MRS)	- Analyzes concentrations of brain metabolites.	- Detects biochemical changes in lesions & normal-appearing brain tissue.	- Assessment of neuronal loss, inflammation, and gliosis.
- Susceptibility Weighted Imaging (SWI)	- Utilizes magnetic susceptibility differences between tissues.	- Sensitive to iron deposition and microbleeds.	- Investigation of chronic active lesions and iron accumulation.
- Perfusion MRI	- Measures cerebral blood flow and volume.	- Assesses inflammatory activity and vascular changes.	- Evaluation of active lesions and disease activity.

Three-Dimensional Phase-Sensitive Inversion Recovery (PSIR):

Although 3D Phase-Sensitive Inversion Recovery (PSIR) is still relatively underutilized in clinical practice, growing evidence suggests it offers clear advantages over traditional imaging techniques for detecting MS lesions in the spinal cord. One study, for instance, found that 3D PSIR detected substantially more lesions than the combined dataset of 3D Short Tau Inversion Recovery (STIR) and T2-weighted imaging 371 lesions compared to just 173, a statistically significant difference ($p<0.05$) [33]. Numbers like that are hard to ignore, and they strongly suggest that newer MRI sequences may offer much greater sensitivity for spinal cord pathology than conventional approaches like proton density-weighted imaging.

Interestingly, phase-sensitive inversion recovery (PSIR) appears to perform similarly to double inversion recovery (DIR) imaging in terms of detecting lesions, achieving 23.7% sensitivity and 88.3% specificity in one comparative study [37]. Some reports even hint that PSIR might slightly outperform DIR although it is important to note that this advantage has not yet been confirmed

through histopathological validation [37]. I think these findings are encouraging, but they also highlight the critical need for larger studies, ideally with pathological confirmation, before PSIR can be fully embraced as a clinical gold standard for spinal cord imaging [56-62].

Conclusion:

Magnetic resonance imaging remains the cornerstone of multiple sclerosis diagnosis and management, with conventional sequences such as T2-FLAIR and gadolinium-enhanced T1 imaging forming the essential diagnostic backbone. Advanced MRI techniques ranging from double inversion recovery and susceptibility-weighted imaging to ultra-high-field MRI offer substantial improvements in the detection of cortical, spinal, and otherwise “invisible” pathology. These modalities promise not only earlier and more precise diagnosis but also a deeper understanding of disease mechanisms, including neurodegeneration, inflammation, and network reorganization.

Despite these advances, challenges remain. Limited availability, technical complexity, and the need for standardized acquisition and interpretation protocols currently restrict the routine clinical use of many advanced sequences. Moreover, the growing recognition of risks such as gadolinium retention demands that imaging strategies balance sensitivity with safety.

Looking forward, the integration of quantitative imaging biomarkers, higher-field strength imaging, and artificial intelligence-assisted analysis represents a pivotal opportunity to transform MS care. Future research must focus not only on technical validation but also on demonstrating how advanced imaging improves patient outcomes, informs treatment decisions, and personalizes disease monitoring.

Ultimately, bridging the gap between emerging imaging science and routine clinical practice will be essential. As MRI technology continues to evolve, interdisciplinary collaboration among radiologists, neurologists, physicists, and data scientists will be critical to fully realizing MRI’s potential in reshaping the landscape of MS diagnosis, prognosis, and therapy.

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مراجعة لإرشادات التصوير بالرنين المغناطيسى التشخيصى للتصلب المتعدد

تم إجراء مراجعة فى مصر خلال الفترة من فبراير ٢٠١٠ إلى فبراير ٢٠٢٥، بهدف تقييم إرشادات التصوير بالرنين المغناطيسى لتشخيص التصلب المتعدد، مع مقارنة البروتوكولات التقليدية بالتقنيات الحديثة لتحسين دقة التشخيص وتوجيه الممارسات السريرية المستقبلية.

اعتمدت المراجعة على تحليل الإرشادات الدولية الحديثة مثل معايير ماكدونالد ٢٠١٧ وتوصيات MAGNIMS–CMSC–NAIMS لعام ٢٠٢١، إضافة إلى استعراض دراسات تناولت تقنيات متقدمة مثل التصوير المزدوج العكسى، التصوير بالترجيح المغناطيسى، تصوير الانتشار، تصوير نقل التمغنط، التصوير بالرنين المغناطيسى عالى الدقة (٧ تسلا)، والتصوير الوظيفى، وكذلك استخدام الذكاء الاصطناعى فى تحليل صور الرنين.

أظهرت النتائج أن التصوير التقليدي باستخدام تسلسلات مثل T2/FLAIR والرنين المعزز بالجادولينيوم لا يزال أساسياً للتشخيص بسبب فعاليته فى كشف آفات المادة البيضاء. لكن هناك حاجة لاستخدام تقنيات حديثة لتحسين الكشف عن الآفات القشرية والتمييز بين أنواعها. أبرزت المراجعة أن تقنيات مثل التصوير المزدوج العكسى توفر وضوحاً أكبر للآفات القشرية، والتصوير بالترجيح المغناطيسى يساعد فى تحديد علامة الوريد المركزى كمؤشر مميز للتصلب المتعدد. كما أن استخدام أجهزة ٧ تسلا حسّن الكشف عن الآفات الصغيرة، بينما قدمت تقنيات الانتشار ونقل التمغنط مؤشرات كمية دقيقة لتقييم تضرر البنية العصبية.

خلصت الدراسة إلى أن البروتوكولات التقليدية لا تزال مهمة، لكن دمج التقنيات المتقدمة والذكاء الاصطناعى يمكن أن يعزز دقة التشخيص، ويساعد على تقييم تقدم المرض، ويمهد لاعتماد نهج تشخيصى أكثر شمولية يجمع بين الطرق التقليدية والحديثة.